

## **REMARKS/ARGUMENTS**

### **Status of the Claims:**

Claims 1 – 27 are pending. Claims 1 – 4, 9, 11 – 14, 17, 20, 23 and 24 have been rejected. Claims 5 – 8, 10, 15, 16, 18, 19, 21, 22 and 25 – 27 have been objected to.

Claims 5 – 7, 21 – 22 and 25 have been amended to cure objections related to multiple dependent claims.

Claim 4 has been amended voluntarily to correct inadvertent typographical and grammatical errors. Claims 7 – 9, 15 – 17, 20, 23, and 25 – 27 have been amended voluntarily to remove reference numerals. Claims 1 – 11 and 16 have been amended voluntarily for editorial purposes, primarily to delete the term “step”. No new matter has been added by these voluntary amendments.

### **Allowable Subject Matter:**

Applicants note the indication of allowable subject matter in claims 18 and 19.

### **Claim Objections:**

The Examiner has objected to claims 5 – 8, 10, 15, 16, 21, 22 and 25 – 27 under 37 CFR 1.75(c) as being in improper form because a multiple dependent claim cannot depend upon another multiple dependent claim.

Claim 5 has been amended to remove the dependence from multiple dependent claim 4, thus curing the objection to claim 5.

Claims 6 and 7 have been amended to depend solely from claim 1, thus curing the objections to claims 6 – 8, 10, 15 and 16.

Claim 21 has been amended to depend from claim 17 or claim 18, thus curing the objection to claim 21.

Claim 22 has been amended to depend solely from multiple dependent claim 19, thus curing the objection to claim 22.

Claim 25 has been amended to depend solely from claim 17, thus curing the objection to claim 25.

**Claim Rejections under 35 U.S.C. 112:**

The Examiner has rejected claims 11 – 14 under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The Examiner alleges that the specification fails to describe the frequency domain and notch as they pertain to the applied signal recited in claims 11 – 14. Applicants respectfully traverse this rejection in view of the remarks that follow.

Support for the “frequency domain” and “notch” limitations of claims 11 – 14 may be found at page 19, lines 14 – 22 and Figure 4 of the instant application. Accordingly, Applicants respectfully request that the rejection of claims 11 – 14 under 35 U.S.C. 112, first paragraph, be withdrawn.

The Examiner has rejected claims 11 – 14 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Examiner alleges that there is insufficient antecedent basis for the limitation “the frequency domain” in claims 11 – 14. Claim 11 has been amended to recite “a frequency domain”, thus overcoming the rejection under 35 U.S.C. 112, second paragraph.

**Claim Rejections under 35 U.S.C. 102:**

The Examiner has rejected claims 1 – 4, 9, 17 – 20 and 23 – 24 under 35 U.S.C. 102(b) as being anticipated by Whitehouse et al. (U.S. Patent No. 6,011,259). Applicants respectfully traverse this rejection, in view of the remarks that follow.

*“A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference.” (MPEP 2131)*

Claim 1 as amended recites “(1) subjecting a stream of ions to a first mass analysis at a pressure no higher than approximately  $2 \times 10^{-5}$  torr, to select ions having a mass-to-charge ratio in a first desired range; (2) passing the selected ions into a radio frequency linear ion trap (Q2) containing a gas”. In other words, mass analysis of the stream of ions is performed prior to injecting the selected ions into the linear ion trap for isolation. The first mass selection is performed in a different apparatus than the apparatus of the linear ion trap.

Claim 17 as amended recites "*a first mass analyzer (Q1) at a pressure no higher than approximately 2x10<sup>-5</sup> torr to select ions having a mass-to-charge ratio in a desired range; a radio frequency linear ion trap (Q2) to receive the selected ions*".

Whitehouse et al. does not disclose, either expressly or inherently, the above-quoted limitations of amended claims 1 and 17.

Whitehouse et al. teaches "a linear multipole ion guide ... configured to operate with m/z range selection, trapping and subsequent ion fragmentation using CID within the multipole ion guide. Parent ions and multiple generations of fragment ions formed within the ion guide are subsequently Time-of-Flight mass analyzed." (col. 7, line 64 – col. 8, line 6) "The invention includes the operation of the multipole ion guide to selectively trap, fragment and transmit ions to the pulsing region of a TOF mass analyzer to achieve MS/MS" functionality in a TOF mass analyzer apparatus interfaced to an API source." (col. 8, lines 36-40)

The Examiner has referred to quadrupole elements 110 and 111 of Whitehouse et al. Whitehouse et al. teaches using a first multipole ion guide (110) at high pressure as a first mass selecting ion trap and collision cell (col. 21, lines 56-59) and using a second multipole ion guide (111) as a second mass selecting ion trap and collision cell. While these might, on superficial review, appear to provide a structure similar to the present invention, it is clear that Whitehouse teaches that both should be operated at a relatively high pressure, as detailed below. In relation to the first quadrupole 110, it is noted (column 21, lines 56-58): "Due to the higher pressure in the ion guide 110...ion fragmentation can occur due to CID of ions with the neutral background gas...". As detailed in the present specification, e.g. at amended page 3, lines 17-19, commenting on WO 98/06481 which is equivalent to the cited Whitehouse et al. reference, "this is a distinct disadvantage, since a multipole ion guide used both for ion isolation and mass analysis has a relatively low resolution." It is further noted, towards the bottom of page 3 of the present specification, that this low resolution is due to (1) the high pressure and (2) choice of gas. In contrast, in the first mass analyzer, conditions are provided, notably a low pressure, to enable high resolution mass selection to be effected.

Whitehouse et al. makes reference, in relation to Figure 1, to an "ion selection trapping mode" (col. 20, lines 63-64) where ions are injected into the trapping ion guide for ion selection and isolation. This ion guide first traps and isolates the ions followed by performing a mass selection in the same ion guide before releasing the ions into the second ion guide.

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Although Whitehouse et al. discloses "ion guide 110 can be operated in a wide m/z range trapping mode and ion guide 111 in a m/z selective trapping mode" (col. 22, lines 4-6), the ion guide 110 "operates in a background pressure typically maintained between 5x10-4 and 1x10-2 torr" (col. 21, lines 46-48). Therefore, even if one were to consider ion guide 110 as "a first mass analyzer" and ion guide 111 as "a radio frequency linear ion trap", ion guide 110 is not "at a pressure no higher than approximately 2x10-5 torr", as recited by amended claim 17, and in no sense provides a low pressure high resolution mass analyser.

The pressure of the first mass analyzer is not a simple design choice. As explained on page 3, lines 11-33 of the instant application, using an ion guide for both ion trapping and mass analysis requires a high pressure, which results in relatively low resolution. In contrast, operating a mass analyzer purely as a mass analyzer at a low pressure, such as, for example, 2x10-5 torr, results in a mass resolution that may be in the thousands.

Consequently, Whitehouse et al. does not describe, either expressly or inherently, the above-quoted limitations of claims 1 and 17 and therefore Whitehouse et al. cannot anticipate claim 1 or claim 17. Claims 2 – 4 and 9 depend from claim 1 and include all the limitations of the independent claim. Therefore, Whitehouse et al. cannot anticipate claims 2 – 4 and 9. Claims 18 – 20 and 23 – 24 depend from claim 17 and include all the limitations of the independent claim. Therefore, Whitehouse et al. cannot anticipate claims 18 – 20 and 23 – 24.

Applicant respectfully requests that a timely Notice of Allowance be issued in this case.

Respectfully submitted,



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